REMARKS

This application is responsive to the Office Action mailed on November 2, 2004, and is accompanied by a one-month extension of time along with an authorization to charge account No. 50-0951 for the extension. A Rule 131 Declaration from Inventor Dr. Whitten accompanies this Reply which evidences conception of the invention back to at least September 30, 1999 along with reasonable diligence from this date until the filing date of the present application.

In this Reply, claims 1, 7 and 13 have been amended. No new matter has been added.

Claims 1 and 6-13 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Cooks et al. (U.S. 6,762,406) in view of Stafford et al. (U.S. 4,540,884) or Hashimoto et al. (U.S. 6,423,965).

Claims 2-5, 14 and 15 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Cooks et al. in view of Stafford et al. or Hashimoto et al., and further in view of Clemmer et al. (U.S. 5,905,258). Alternatively, these claims are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cooks et al. in view of Stafford et al. or Hashimoto et al., and further in view of Batemen et al. (U.S. Publ. No. 2003/0001084).

Before reviewing the cited art, Applicants will first review the claimed invention as now recited in amended claim 1. Amended claim 1 recites an ion trap-based system for chemical analysis including an ion trap array. The ion trap array comprises a plurality of ion traps arranged in a 2-dimensional array for initially confining ions. Each of the ion traps comprise a central electrode having an aperture, a first and second insulator each having an aperture sandwiching the central electrode, and first and second end cap electrodes each having an aperture sandwiching the first and second insulator. A structure is provided for simultaneously directing a plurality of different species of said ions out from at least one of the ion traps. A spectrometer

including a detector is provided for receiving and identifying the ions based on arrival times. The claimed system now recites *a drift region or drift channel disposed between the end cap electrode and the detector*. The drift region has a length sufficient for resolving arrival times of different species of the ions. The claimed system is suitable for both time of flight mass spectrometry (TOF) systems and ion mobility spectrometry (IMS) systems.

[0001] Both TOF and IMS systems require a sufficient length for ions exiting the traps to drift to operate. Regarding TOF, at certain discrete times, generally denoted as t=0, the ions are accelerated by an applied electric field imposed between an acceleration grid the trap where the ions initially reside. The ions are then allowed to drift in an essentially zero electric field region located between the acceleration grid and the detector until they reach the detector. The arrival time of the ions is related to their mass because the heavier ions achieve a lower velocity while in the acceleration zone as compared to lighter ions.

[0002] Ion mobility spectrometry (IMS) is another form of chemical analysis that is similar to TOF mass spectrometry, but identifies chemical species based on drift time through a drift region generally referred to as a drift channel. The mechanical arrangement for IMS is essentially the same as in TOF. Ions start at t = 0 in a confined region, such as a trap in the claimed invention, and are then are allowed to drift through a constant field region to a detector, with an arrival time inversely proportional to the ion mobility. IMS is performed at higher pressure, even atmospheric pressure, versus a high vacuum for TOF-mass spectrometry. The gas that is present in IMS causes a viscous drag on the ions so it is necessary to have an electric field in the drift region. The ions move through the drift region with a velocity that is proportional to the electric field. The proportionality constant is characteristic of the ion but not quite as

informative as the mass. Also, the resolution is degraded because of the diffusion that takes place during the drift.

Cooks is the primary reference cited and is entitled "Ion trap array mass spectrometer" and discloses a mass spectrometer having an array of parallel and/or tandem ion traps. The ion traps are preferably formed by providing a body of conductive material with a plurality of holes forming ring electrodes and electrodes on opposite faces of the body, opposite the ends of said ring electrodes, to define with the ring electrodes a plurality of parallel ion traps. Applicants note that Cooks does not mention IMS anywhere. This is quite logical because his operation is always disclosed to be in a high vacuum, a high vacuum being incompatible with IMS which requires a relatively high pressure to provide the necessary viscous drag on the ions.

Cooks cleverly uses the ion traps to both trap ions, as well as a mass analyzer/spectrometer as suggested by the title of the invention "Ion trap array mass spectrometer". Such an arrangement simplifies the mass spectrometry system as well as its operation. Specifically, as noted relative to FIG. 6A-C an a scanned rf voltage is applied to the trap, with different ions becoming ejected from the trap at different rf voltages (with a further effect regarding the size of the traps):

> FIGS. 6A-6C show the results of an experiment that demonstrates the effect of trap dimensions on mass range using a two CIT array with a trap of 5.0 mm radius and a trap of 6.0 mm radius. In each case the length of the cylindrical electrodes was 6.80 mm. These data represent the reduction to practice of the basic concepts underlying the first embodiment. *FIG. 6A shows the spectrum for a sample obtained by scanning the amplitude of the rf voltage* for a trap having 5.0 mm radius. *FIG. 6B shows the spectrum of the same sample obtained by scanning the amplitude of the rf voltage* for a trap having 6.0 mm radius. FIG. 6C shows a spectrum recorded from both traps operated by scanning the rf simultaneously with a single electron multiplier detector. *This shows how the relative size of the traps causes ions of the same mass/charge ratio to become unstable at different times, corresponding to different values of the rf amplitude. This results in a separation of the signals due to ions of a given mass/charge ratio when the two traps are operated in an array.* The ions from the 5.0 mm radius trap are ejected during a mass selective instability scan before their counterparts in the 6.0 mm radius trap, as seen from the labeling of the peaks in terms of nominal mass-to-charge ratios. This demonstrates

that the r0 and z0 parameters affect the location of the ions of different masses in the stability diagram. *On the basis of these data, it can also be understood how selection of ions of single mass/charge ratios by the chosen isolation method (rf/dc, waveform or other method) will allow ions of different mass/charge ratios to be trapped in different CITs in an array. This permits mass analysis of a sample by trapping ions of different mass-to-charge ratios and then using a pulse to eject the ions into a detector associated with each trap volume.* (italics for emphasis only).

Ejection of trapped ions from the individual ion traps for detection is disclosed to be achievable in a number of ways other than a scanned rf voltage. The detector is always a position sensitive detector (e.g. pixelated detector), such as detector 52 shown in FIG. 8 as described below, which resolves different ions based on the position on the detector that they are received with no regard to the time received. (See FIG. 3A and 3B).

As noted in col. 9, line 28 to 44:

Referring to FIG. 8 by way of example, application of a short dc pulse on the endcap electrode 50 opposite the detector will eject all ions through the mesh-type endcap 51 simultaneously from all traps onto the *position-sensitive detector 52*. The position of the signal correlates with the mass/charge ratio of the ions. Second, ions can be ejected by stepping the rf voltage to a suitably high value (corresponding to qz values in excess of the stability boundary). Third, and least desirably, ejection might be by means of an rf voltage ramp, as is commonly done. In each case, detection can be by means of a *position-sensitive array detector*, or, for experiments in which the objectives are limited, by point detectors (e.g. an electron multiplier or Faraday cup). The first and second mode of ion ejection provide a simpler method than the rf voltage ramp, and therefore allow use of the invention with a smaller control electronics package.

The distance between the trap array and the detector is purposely kept short by Cooks to minimize the potentials required for system operation. However, for both TOF or IMS, it is necessary to perform a drift time measurement in the separation region. In Cooks' description, there is no mention of a way to determine the transit time of the ions as they pass through/across the separation region. Being short, the separation region disclosed by Cooks clearly cannot serve as a TOF mass spectrometer or IMS.

According to the Examiner, on page 3 of the Office Action, Cooks can be modified by adding a separate spectrometer tandem to the trap array:

> Although Cooks' ion trap system does not explicitly recite a specific type of (mass) spectrometer, each of the ion trap itself is basically a mass (m/z) analyzer, as recited in Col.9/l.9/l.27-44. Furthermore, it is generally also known in the art that an auxiliary mass spectrometer can be added in tandem to a first stage of Cooks' ion trap array 44-42-46 shown in Fig.8, e.g., replacing the second ion trap array 50-48-51.

Applicants respectfully disagree with the assertion above. As noted earlier, Cooks' ion trap array is used both to trap ions and as a mass analyzer in conjunction with a position sensitive detector. Since the Cooks' system already includes a mass analyzer, it would be <u>pointless</u> to add <u>another mass spectrometer</u> in the form of an auxiliary mass spectrometer. Accordingly, Cooks clearly teaches away from such an addition and/or modification to add an auxiliary mass spectrometer

Alternatively, on page 5 of the Office Action, the Examiner asserts that it is obvious to replace the second ion trap in a two ion trap array system where the first and second ion trap are connected in series with either a TOFMS or IMS:

> ► Regarding claims 2, 3, 14 and 15, it is generally known in the art that an auxiliary mass spectrometer can be added in tandem to a first stage of Cooks' ion trap array 44-42-46 shown in Fig.8, e.g., replacing the second ion trap array 50-48-51, as already recited previously. This auxiliary spectrometer may be in the form of either a time-of-flight mass spectrometer (TOFMS) or an ion mobility spectrometer (IMS), or both, as

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recited by Clemmer et al. in the Abstract/lines 1-13. As shown in Fig. 4, Clemmer's TOFMS is shown by ref. no. 36 and the IMS is shown by ref. no. 34, as recited in Col.6/ll.24-46.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an auxiliary spectrometer in sequence to Cooks' first ion trap array 44-42-46 shown in Fig.8, i.e., replacing Cooks' second ion trap array 50-48-51 with Clemmer's IMS 34 and/or TOFMS 36, since those mass spectrometer types are simpler to operate than Cooks' quadrupole ion trap, as generally known in the art.

Similarly, According to the Examiner on page 7 of the Office Action:

3. Claims 2-5, 14 and 15 are *alternatively* rejected under 35 U.S.C. 103(a) as being unpatentable over Cooks et al. in view of Stafford et al. or Hashimoto et al., and further in view of Bateman et al. (US-PGPUB 2003/0001084).

Cooks et al. in view of Stafford et al. or Hashimoto et al. show all the limitations of claims 2-5, 14 and 15, as previously applied to their parent claims 1 and 8-13, except for specific claim limitations that are all rendered obvious by Bateman et al., as recited in sect. [0090] and [0091] in reference to Fig.6 and sect. [0112] to [0115] in reference to Fig.8, wherein the ion trap is shown by ref. no. 2, the IMS by ref. no. 4 and the TOFMS by ref. no. 11.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an auxiliary spectrometer in sequence to Cooks' first ion trap array 44-42-46 shown in Fig.8, i.e., replacing Cooks' second ion trap array 50-48-51 with Bateman's IMS 6 and/or TOFMS 11, since those auxiliary mass spectrometer types are simpler to operate than Cooks' quadrupole ion trap, as generally known in the art.

Firstly, as noted above, there is no motivation to modify Cooks' system as it already provides an ion trap array which functions as a trap and as a mass spectrometer. Moreover,

Applicants respectfully traverse the examiner's assertion that IMS and TOFMS are "mass spectrometer types [that] are simpler to operate than Cooks' quadrapole ion trap, as generally known in the art". Cooks emphasizes in his objects of the invention (col. 3, lines 24-31) the simplicity of his system and associated operation:

> It is an object of the present invention to provide a mass spectrometer consisting of an array of quadrupole ion traps each element of which is operated using the same rf and dc trapping signals.
>
> It is another object of the present invention to provide a mass spectrometer having simple miniaturized control electronics and pumping systems.

Cooks' position sensitive detectors simplify operation by removing the need to resolve based on arrival time. TOF and IMS require different electronics circuitry than ion trap mass spectrometry that is based on radiofrequency voltages. By using tandem ion traps, Cooks can use the same electronics circuitry for both mass analyzers and does not need the circuitry for drift time measurement used for TOF/IMS. Accordingly, *assuming arguendo feasibility of such an arrangement,* substituting a TOF or IMS spectrometer for Cooks' second spectrometer would add both system and operation complexity. Therefore, there is clearly no motivation for the proposed combination.

Secondly, *notwithstanding the redundancy and lack of motivation issue,* Cooks does not provide a drift region or drift channel disposed between trap and the detector having a length sufficient for resolving arrival times of different species of the ions. As a result, a TOF or IMS spectrometer would not be operable if substituted for the second trap array because sufficient drift time would not be provided in the short distance between the last trap array and the detector to permit ion identification based on arrival time.

In contrast, amended claim 1 recites an ion trap-based system for chemical analysis suitable for both time of flight mass spectrometry (TOF) systems and ion mobility spectrometry

(IMS) including an ion trap array, and a spectrometer including a detector for receiving and identifying the ions *based on arrival times, and a drift region or drift channel disposed between the end cap electrode of the trap array and the detector*. The drift region has a length sufficient for resolving arrival times of different species of the ions. Since Cooks' "Ion trap array mass spectrometer" uses the trap array as a spectrometer, and lacks a drift region between the trap array and the position sensitive detector making a substitution of an IMS or TOFMS therein inoperable, Applicants submit that amended claim 1 and its respective dependent claims are patentable over the cited art.

Certain dependent claims are believed to recite independently patentable limitations. For example, claim 3 recites the spectrometer comprises an ion mobility spectrometer (IMS). Ion mobility is <u>not</u> a mass spectrometer as it does <u>not</u> depend solely on the mass of the ion, but also depends on the size and structure of the ion. Thus, the class of potential "auxiliary mass spectrometers" does not include IMS.

Amended claim 7 is dependent on claim 3. Amended claim 7 recites r_0 and z_0 are both less than 1.0 mm. Such sizes are at least 5x smaller than disclosed by Cooks. Although as correctly noted by the Examiner that size modification is generally not the basis for patentability, claim 7 recites an arrangement that one having ordinary skill in the art would not expect to be operable based on the high pressure required by IMS together with the sub-millimeter apertures. There is a size constraint imposed by operating ion traps at pressures other than vacuum. That is that the trap size should be comparable to or smaller than the mean free path of an ion in the gas for efficient trapping. This size condition is also the requirement for avoiding electrical breakdown between the trap electrodes. If the spacing between the electrodes is greater than a mean free path, the ions can accelerate to sufficient kinetic energy between collisions that they

can cause an avalanche ionization process resulting in a discharge. Cooks' traps are operated at low pressure where electrical breakdown is not a problem, thus the larger size is preferred as it is acceptable. Accordingly, amended claim 7 is believed to recited independently patentable subject matter.

Method claim 13 has been amended to recited limitation analogous to those recited in amended system claim 1. Claim 13 now recites "simultaneously directing a plurality of different species of said ions out from at least one of said (2D) ion traps into a drift region or drift channel disposed between said trap array and a detector, said drift region or drift channel having a length sufficient for resolving arrival times of different species of said ions" and "identifying said ions based on arrival times of different species of said ions reaching said detector". In view of the above remarks relative to amended claim 1, Applicants submit that amended claim 13 and its respective dependent claims are patentable over the cited art.

Although not believed to be required for patentability, as a separate and independent grounds for patentability of the claimed invention, Applicants have also provided a Rule 131 Declaration from Inventor Dr. Whitten which evidences a date of conception back to at least September 30, 1999, along with diligence until the filing date of the present application. The Declaration is accompanied by a copy of a Quarterly Report dated September 30, 1999 (Marked exhibit "A") that was submitted to DOE headquarters on approximately Oct. 10, 1999 that describes some initial experiments with trap arrays according to the invention.

The Quarterly Report demonstrates proof of conception for the claimed subject-matter of Applicants' invention at least as early as September 30, 1999. This date predates the dates afforded to Cooks and Bateman patents as references, that being May 25, 2000 and March 1, 2002, respectively.

As noted in the declaration, the Quarterly Report is a standardized filing utilized by the Oak Ridge Labs. Experiments were run by the inventors from summer 1999 through 2002 were used to identify preferred components and conditions. An invention disclosure was submitted to the office of General Counsel, Intellectual Property during the fall 2002, and was signed by Shelley Stafford from the General Counsel, Intellectual Property Office on December 6, 2002. Once an Oak Ridge invention disclosure form is completed, the disclosure is reviewed by an invention review board to determine whether to prepare an application based upon the submitted disclosure. Upon reaching a decision to prepare an application, outside counsel is selected to prepare the application. The undersigned was authorized to file a patent application based on the present invention on May 7, 2003. Instructions in this regard, together with the invention disclosure form, are conveyed to the outside counsel. The outside counsel prepares a draft of the application that is iteratively reviewed by each inventor until such time that the inventors are satisfied that the application sufficiently details the inventive concepts detailed in the disclosure, at which time the application is expeditiously filed with the USPTO.

Applicants thus exercised reasonable diligence from the date of conception which is prior to the effective date of Cooks as a reference until the March 16, 2004 filing date of the instant application. Since Applicants conceived of the present invention before the effective date of Cooks and exercised diligence in constructively reducing the invention to practice between the date of the Disclosure until the filing date, as supported by the enclosed Declaration, Cooks should be withdrawn as a reference.

Applicants have made every effort to present claims which distinguish over the cited art, and it is believed that all claims are now in condition for allowance. However, Applicants

request that the Examiner call the undersigned (direct line 561-671-3662) if anything further is required by the Examiner prior to issuance of a Notice of Allowance for all claims.

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Respectfully submitted,

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